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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,059	12/31/2001	Ton Logtenberg	313632000801	9790

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EXAMINER	
MCGILLEM, LAURA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,059	LOGTENBERG ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-16,22,23 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-16,22,23 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/418,563.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 8-16, 22-23 and 27-29 are pending. Claims 5-7 are now canceled and claims 27-29 have been added in the response filed 3/21/05. Claims 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/21/2005.

It is noted that rejection of claims 1-2, 4-5, 7-9, 11-12, 14-16 and 22-23 under 35 U.S.C. 102(b) as anticipated by Tykocinski et al (WO 96/12009 A2) is traversed. Tykocinski et al teach a process for providing a cell or cell membrane with an additional proteinaceous molecule, the process comprising contacting the cell or membrane with a lipid-modified proteinaceous molecule, where the lipid-modified proteinaceous molecule comprises at least one protein moiety derived from a first protein and at least one lipidation signal derived from a second protein.

The present claims have been amended in a response filed 3/21/05 and are now drawn to a proteinaceous molecule having a lipidation signal that is specifically derived from a bacterial protein. Tykocinski et al does not teach a lipidation signal derived from a bacterial protein, instead, the preferred lipid modification is a eukaryotic lipophilic anchor glycophosphatidylinositol (GPI) modification. In addition, the described fusion protein was expressed in *D. melanogaster* cells and not in *E. coli* cultures. Tykocinski et

al no longer anticipates claims 1-2, 4-5, 7-9, 11-12, 14-16 and 22-23. The rejection is withdrawn.

It is noted that in the response filed on 3/21/05, claims were amended in response to rejection of claims 1-16 and 22-23 under 35 U.S.C. 112, second paragraph. Claims were rejected for inclusion of the phrase "derived from" in regards to cell membranes and proteins. Applicant has amended claim 1 as recommended in the office action filed 5/18/04 by changing "derived from" to "obtained from" with regard to membrane only.

Applicant has retained the phrase "derived from" with regards to proteinaceous molecules and argues that the phrase "derived from" is aptly descriptive of the proteins of the invention because the proteinaceous molecules have been produced by a multistep process. Applicant's arguments filed 5/18/04 have been fully considered but they are not persuasive. Despite the Applicant's argument to the contrary, the phrase "derived from" is unclear because the language suggests that the claimed proteinaceous molecules have been somehow altered in the multistep production process. The phrase "obtained from," suggests that the proteinaceous molecules have been produced from the starting polypeptide sources without alteration to the amino acid sequence. If Applicant intends that the proteinaceous molecules have actually been "derived from" the original polypeptide sources, the metes and bounds of the changes to the proteinaceous molecules have not been adequately described and

therefore the claims are unclear. It is noted that claims 16 and 22-23 contain the phrase "membrane derived from" and were not amended. Rejections of claims 1-4, 8-16 and 22-23 are maintained.

Specification

The specification is objected to because of the following informalities: the section Brief Description of Drawings is not properly titled. The section of the specification entitled Legends to the Figures (see paragraph 0087) should be re-titled to read Brief Description of Drawings.

The specification is objected to because in the improperly titled Legends to the Figures, the case of the letters identifying the panels in Figure 1, 6 and 9-10 does not match the case of the letters in the drawings. In the Brief Description, the letters identifying the panels are lower case letters, while in the drawings the letters identifying the panels are capital letters. Appropriate correction is required.

The specification is objected to because the nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 as follows: Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in

the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

The specification includes an amino acid sequence which does not have a corresponding SEQ ID NO listed. (see paragraph 0038). Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 8-16, 22-23 and 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **The rejections of claims 27-29 are new rejections necessitated by amendment filed 3/21/05.**

Claims 1-4, 8-16, 22-23 and 27-29 recite the phrase "derived from" in the context of cell membranes and portions of first and second proteins making it unclear the nature and number of steps required in order to obtain a "derivative" of a protein and/or membrane. Examiner suggests replacing the phrase "derived from" with the phrase "obtained from". The phrase "derived from" implies an indirect process, while the phrase "obtained from", implies a more direct process for obtaining the desired products.

Claim 23 recites the limitation "one additional lipid-modified". There is insufficient antecedent basis for this limitation in the claim. Claim 23 is an independent claim drawn to a cell or particle and there is no prior mention of a lipid–modified molecule in the claim. Therefore, the metes and bounds of the phrase "one additional" is not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 8-16, 22-23, 27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by de Kruif et al (FEBS Lett. (1996). Vol 399, pgs 232-236). **Rejection of claims 27-29 are new rejections necessitated by applicant's amendment filed 3/21/2005**. Claims 3, 10-11, 15, and 28 are rejected as being dependent on a rejected claim. The Applicants claim a process for altering the properties of a cell and/or a particle comprising a membrane obtained from a cell said process comprising the step of contacting said cell and/or said particle with a lipid-modified proteinaceous molecule, wherein said lipid-modified proteinaceous molecule comprises at least one protein moiety derived from a first protein and at least one lipidation signal derived from a second protein where said second protein is a bacterial protein and is partially assembled in a cell. Applicants also claim that part of the proteinaceous molecule is

derived from a protein of the immune system, including a single chain variable antibody fragment or an antigen binding Fab fragment and includes a purification tag. The Invention also comprises a cell, eukaryotic cell or a particle comprising a membrane derived from said cell, to which a lipid modified proteinaceous molecule has been added. The specification teaches addition of a second or even more lipidation signals, to result in a lipid-modified proteinaceous molecule with two or more lipid tails. However, it does not specify whether the bacterial lipidation signal must be derived from the first or the second protein nor does it mandate an order in which the first and second protein be expressed on the lipid modified proteinaceous molecule.

de Kruif et al teach that DNA encoding portions of human-specific CD22 antibodies known as single chain Fv (scFv) fragments were fused to a bacterial lipoprotein sequence and a hexahistidyl tag and cloned into a vector for expression in *E. coli* cultures (see page 232, column 2, paragraph 2, in particular) which reads on a lipid-modified proteinaceous molecule where at least one protein moiety is derived from a protein of the immune system such as a single chain variable fragment (ligand), and the second protein is a bacterial protein. It also reads on part of the assembly of the proteinaceous molecule occurring in a cell and at least one lipidation signal derived from a second bacterial protein. The hexahistidyl tag reads on a purification tag.

The CD22-specific scFv lipoprotein was then purified and coupled to liposomes to create immunoliposomes (See page 233, paragraphs 2.4-2.5, in particular). The

immunoliposomes were incubated with CD22+ B-lineage cells and specifically bound to CD22+ B cells, fused with the membrane and were internalized (see page 234, paragraphs 3.4 and 3.6, in particular) which reads on contacting a cell with a lipid-modified proteinaceous molecule and adding a lipid-modified proteinaceous molecule to the membrane of a eukaryotic cells. Fusion of the CD22-specific scFv lipoprotein containing liposome with the B cell membrane necessarily creates a human cell comprising a lipid-modified proteinaceous molecule which reads on a eukaryotic cell comprising a lipid-modified proteinaceous molecule according to claim 1 wherein said lipid-modified proteinaceous molecule comprises at least one protein moiety derived from a first protein and at least one lipidation signal from a second protein where second protein is a bacterial protein. Since the instant disclosure does not specify the bacterial lipidation signal from the first or second protein as discussed above, de Kruif et al also reads a molecule comprising one bacterial lipidation signal from a first protein and at least one protein moiety derived from a second protein.

The limitation imposed by the phrase "at least one additional lipid modified proteinaceous molecule" recited in claim 23 is indefinite, as discussed above. The claim as written could be interpreted to read on a cell comprising more than one lipid-modified proteinaceous molecule wherein the lipid-modified proteinaceous molecules are the same, as opposed to additional multiple lipid-modified proteinaceous molecules that are comprised of different protein moieties or different lipidation signals. If interpreted as the former, claim 23 is anticipated by de Kruif et al because it is very likely that multiple

CD22-specific scFv lipoprotein molecules are present in the liposome, rather than one single CD22-specific scFv lipoprotein in the liposome that was contacting the CD22+ B-cells. As discussed above, fusion of the CD22-specific scFv lipoprotein containing liposome with the B cell membrane necessarily creates a cell comprising at least one additional lipid-modified proteinaceous molecule.

Liposomes comprised of the CD22-specific scFv lipoprotein which specifically bound to the CD22 receptor on the B cells caused enhanced CD22 receptor internalization in the endocytotic pathway (see page 235, column 2, paragraph 2, in particular) which reads on altering the properties of a cell (by enhancing and activating the endocytotic pathway) by a process comprising contacting a cell with a lipid-modified proteinaceous molecule and also reads on part of the proteinaceous molecule which can interact with a signal transducing molecule (CD22) present on the plasma membrane of the cell. Therefore, de Kruif et al anticipate all of that is taught in the listed claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura McGillem
6/10/05

DAVID GUZO
PRIMARY EXAMINER